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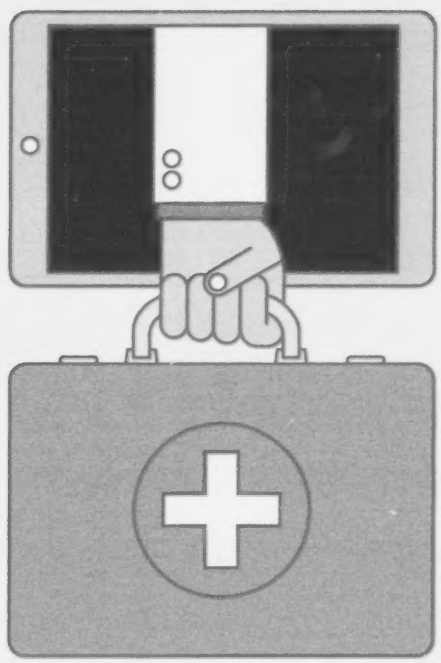
CANADA COMMUNICABLE DISEASE REPORT

INDIGENOUS HEALTH



Overview

Using technology to improve health care in remote Indigenous communities 120

Commentary

What are syndemics and what can be done to address them? 125

Evaluation

Timeliness of communicable disease surveillance in some First Nations communities 133

ID News

What happens when viruses infect bacteria? 143

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CANADA COMMUNICABLE DISEASE REPORT

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Contact Us

ccdr-rmtc@phac-aspc.gc.ca
613.301.9930

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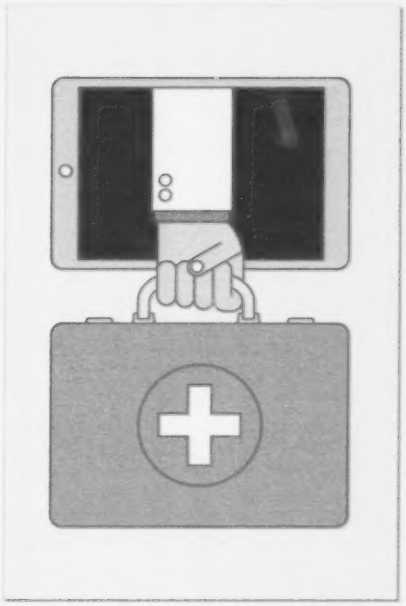

TABLE OF CONTENTS

OVERVIEW

The use of technology to improve health care to Saskatchewan's First Nations communities 120
I Khan, N Ndubuka, K Stewart, V McKinney, I Mendez

COMMENTARY

Outbreaks in the age of syndemics: New insights for improving Indigenous health 125
A Andermann

EVALUATION

Evaluating the timeliness of reporting in a First Nations communicable diseases program 133
A Lam, S Woods, N Ndubuka

ADVISORY COMMITTEE STATEMENT

Summary of the NACI Update on the recommended use of Human Papillomavirus (HPV) vaccine: Nine-valent HPV vaccine two-dose immunization schedule and the use of HPV vaccines in immunocompromised populations 138
SL Deeks, MC Tunis, S Ismail on behalf of the National Advisory Committee on Immunization (NACI)

ID NEWS

Treatment update for hepatitis C virus-Genotype 3 143

Viruses that infect bacteria 143

OVERVIEW

The use of technology to improve health care to Saskatchewan's First Nations communities

I Khan[1]*, N Ndubuka[2], K Stewart[3,4], V McKinney[5] and I Mendez[6]

Abstract

Background: Saskatchewan is a province of over one million people and over 13% are Indigenous peoples, many of whom live on reserve lands. Despite continued efforts, access to health care remains a significant challenge for these Indigenous people, especially those in the North.

Objective: To address this challenge, Saskatchewan's health care providers have been incorporating the use of technology for various health services. This paper describes various ways technology has been used in First Nations communities in Saskatchewan.

Methods: Several pilot projects between First Nations leaders and health care providers, in the communities as well as in the urban setting, have taken place over the past 10 years. Information on these pilots was supplemented with literature reviews and consultations with colleagues at the Northern Inter-Tribal Health Authority, the First Nations and Inuit Health Branch (FNIHB), Health Canada and lead physicians for services to the North.

Results: Numerous technologies have shown promise in aiding the timely delivery of high quality health care. Remote Presence Robotic Technology (RPRT) is a form of telemedicine that creates the sense that a clinician is at the patient's side; enabling clinical services to be provided remotely and in real time. Increasing access to internet services and providing computer tablets to community health nurses have improved patients' access to clinical care and to vital health care information. Robotic ultrasonography has been used to provide onsite care for pre-natal patients. The provision of cell phones to HIV-positive patients has improved compliance with anti-retroviral therapy and has resulted in better clinical outcomes. The Xpert MTB/RIF (*Mycobacterium tuberculosis* complex / resistance to rifampicin) is an automated device that, through analysis of raw sputum samples, can identify the presence of *M. tuberculosis* with greater speed, sensitivity and specificity than the conventional acid-fast bacilli (AFB) smear. Similarly, telemedicine remote communications equipment is being used for patient care across communities. Panorama is a comprehensive, integrated public health information system designed for public health professionals and is currently being introduced in 21 communities in Saskatchewan.

Conclusion: Not only do these innovative technologies appear to improve access and enhance the quality of timely care in remote communities but they also bring comfort to patients, prevent unnecessary transportation and minimize time away from work and family. Although these technologies are not a panacea for some of the determinants of health that can affect the incidence and severity of infectious diseases in First Nations, they do appear to address some of the geographic challenges faced in providing health services in remote communities.

Affiliations

[1] First Nations Inuit Health Branch, Health Canada, Saskatchewan Region, Regina, SK

[2] Northern Inter-Tribal Health Authority, Prince Albert, SK

[3] Saskatchewan Infectious Disease Care Network, Saskatoon, SK

[4] TB Prevention and Control of Saskatchewan, Saskatoon Health Region, Saskatoon, SK

[5] Northern Medical Services, Saskatoon, SK

[6] Department of Surgery, University of Saskatchewan and Royal University Hospital Saskatoon, SK

Correspondence: ibrahim.khan@hc-sc.gc.ca

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Introduction

Saskatchewan is a large province; roughly the size of France. Of the one million people who inhabit the province, over 13% are First Nations (Indigenous), more than half of whom live on reserve land (1-3). Based on 2015 data, Saskatchewan human immunodeficiency virus (HIV) rates are 47 per 100,000 for First Nations people living on south central reserves and 37 per 100,000 for those living on northern reserves (4). Similarly, tuberculosis (TB) rates, addiction trends, HIV-hepatitis C co-infection, chronic diseases (such as diabetes) and traumatic injuries in Saskatchewan First Nations people remain the highest in Canada (2,4,5). In spite of continued efforts, access to primary and specialized care remains a significant challenge for First Nations people, particularly those in the North. In particular, access to timely diagnosis and procedures have been a concern for a long time in remote and isolated communities (2,3,5). Difficulty in accessing health services has had the greatest impact on the most vulnerable segments of the population, including children, pregnant women and the elderly (2,3,5).

Health Canada, Northern First Nations, local physicians and health authorities across the province have been exploring innovative ways to deliver health care services in the remote northern areas (5,6,9). This effort has led to innovative thinking and use of various technologies, including digital and portable diagnostic devices, in the provision of health services in these communities (4-6). The objective of this overview is to describe how technology has been applied to health services in the Northern First Nations communities in Saskatchewan.

Methods

Over the past 10 years, several successful pilot projects in northern communities in Saskatchewan have set the stage for transforming the provision of health services (5-7,11). These pilots included partnering with the First Nations leaders and health care providers, in the communities as well as in the urban setting, to make linkages between on- and off-reserve services possible (6). All authors are involved in a number of these initiatives. Information on these pilot projects was supplemented with literature review and consultations with colleagues at the Northern Inter-Tribal Health Authority, First Nations and Inuit Health Branch (FNIHB), Health Canada and lead physicians for services to the northern communities (5,6,9,11-13,15).

The World Health Organization has defined health technologies as the "application of organized knowledge and skills in the form of devices, medicine, vaccines, procedures and systems developed to solve a health problem and improve quality of lives" (8). Technology has been used in northern Saskatchewan to increase patient access to health care services, increase health professionals access to online resources, assess the potential for long distance diagnostic interventions and improve the care of specific conditions in remote First Nations communities (5,6). For the purpose of this overview, we focused largely on digital technologies and remote and portable diagnostic devices.

Results

Increased patient access to health services

One technology that has been used to increase patient access to care is Remote Presence Robotic Technology that consists of maneuverable robots ("Rosie") and portable devices ("Doc-in-the-box") that enable face-to-face encounters between patients and health care providers despite long distances. The technology, developed in California, uses a regular Wi-Fi phone signal to establish a two-way video link (5,6,9,11-13,15).

Increased health professional access to online resources

The eHealth program of FNIHB (Saskatchewan region) has been supporting the First Nations on reserve communities, and other agencies across the province, to improve connectivity to network services. The majority of the First Nations on reserve communities in Saskatchewan now have access to internet services. A group of community health nurses across Saskatchewan were provided computer tablets to enhance their ability to access online clinical, public health nursing and education tools for patients for whom they provide outreach care. Preliminary results indicate that this pilot project has enabled nurses to have quick access to various resources while using these tablets during provision of mobile/outreach care in the communities (5,7,11).

Assessing the potential for long distance diagnostic technology

There is a significant gap in access to diagnostic services, especially ultrasonography, in First Nations communities. Remoteness and long travel times pose significant challenges in this regard. A pilot study conducted by Dr. Mendez in 2014 used Remote Presence Robotic Technology to assess and treat acutely ill children in Pelican Narrows in central Saskatchewan (6,15). The results demonstrated that the technique was safe, clinically efficacious and cost-effective, with 63% of the acutely ill children treated in their own community. Over the past 10 years, Mendez has been a champion of the use of this remote technique and has run several successful pilots, both in northern communities of Saskatchewan and around the world (5,6,9,11,13). The use of remote-presence robotics and other technologies has set the stage for transforming the provision of health services. There are now 11 medical robots and portable devices in clinical practice in Saskatchewan; more than anywhere else in Canada (9).

Infectious disease doctors in Saskatchewan are also using portable fibroscans for liver clinics on reserves (7). Mendez and many other health care providers have been partnering with First Nations leaders and health care providers, in the communities as well as in urban areas, to fill in the gaps and to link the on- and off-reserve services for First Nations patients (5,6,9,11,12).

The rate of new TB cases has been very high in the northern communities (2,7). In addition to the routine TB screening, a new diagnostic technology, called Xpert-MTBC/RIF (*M. tuberculosis* complex / resistance to rifampin) is being piloted in Northern communities in an effort to offer rapid testing for suspected TB patients (10). If the test is negative, it rules out TB quickly and prevents unnecessary isolation. If the test is positive, it can lead to early diagnosis, rapid initiation of treatment and shorter exposure time of active TB to other community members (17,18).

Telehealth

Telehealth is an internet-based videoconferencing technology used by many health care providers to assess patients and to provide educational sessions and training, as well as for other purposes in various health services and programs. Currently, there are 39 First Nations communities across Saskatchewan where telehealth equipment is available for use (7,16). The number of communities with service and the frequency of telehealth utilization are expected to rise in the coming years across Saskatchewan. **Table 1** summarizes a range of health care goals, together with the telehealth technologies being applied to meet these goals, their application in health care and their preliminary health outcomes.

Table 1: Technologies used to improve health services for First Nations people in Saskatchewan

Goal	Technology	Use in health care	Example of Outcome
Increase patient access to care	Remote Presence Robotic Technology creates the sense that a distant clinician is at the side of the patient, while enabling clinical services to be provided remotely in real time. Also called "Doc-in-the-box"	Used by primary care doctors, nurses, therapists and outreach workers, emergency trauma/ medicine, mental health, pediatricians, counsellors in public health/ HIV clinics	Expedited HIV care and triaging for acute conditions, patient safety and comfort, easy and timely access to health services within the community (5,6,9)
Increase access to online resources for community health nurses/ nurse managers	Tablets used during mobile outreach clinics and visitations	Community health nursing, primary care, medical health officer and mobile outreach teams within the communities	Easy to carry and timely access to online nursing/ clinical/public health and other relevant education resources, improved quality of care and time savings (11)
Improve the care of specific conditions	Internet-based videoconferencing-like technology	Used by many, including health care providers, to assess patients, for educational sessions and trainings and for other purposes in health services and programs	Currently used in 39 health centers across First Nations jurisdictions. Facilitated regular assessment of tuberculosis patients, improved compliance with treatment, increased frequency of follow-up and improved treatment outcomes (7,10, 11,16)
	Cell phones for HIV-positive patients	HIV and TB programs in the communities	Improved attendance at clinics, treatment outcomes and case management, and ensured regular communication with the patients regarding follow-up (9,11)

Table 1: Technologies used to improve health services for First Nations people in Saskatchewan (continued)

Goal	Technology	Use in health care	Example of Outcome
Improve the care of specific condition (con't)	Panorama is a comprehensive, integrated public health information system designed for public health professionals	In immunization programs, it expedited inventory of vaccines and monitoring in the communities. Operated by community health nurses/nurse managers and medical health officers	The system helps professionals work together more effectively to manage vaccination programs, outbreak investigations and family health in 21 communities. More communities to join in the future (7,10)
Improve diagnostics	Robotic ultrasonography for pre-natal care	Prenatal care providers	Improved patient convenience, time, travel and cost, and had less impact on families
	Remote Presence Robotic Technology for point of care diagnosis and treatment	Primary care providers and specialists	Improved patient convenience, time, travel and cost savings, and had less impact on families (5,6,9,11-13,15)
	Portable fibroscan	Nurses specializing in liver health and doctors specializing in infectious diseases	Used for assessment and staging of liver fibrosis in patients with hepatitis B and C (7). Assessment provided within the communities
	Xpert MTB/RIF is a new molecular test for tuberculosis and other conditions	Rapid TB diagnostics	Timely diagnosis of TB and early prevention of possible exposure, recently Installed in northern communities to support TB high incidence strategy (10,17,18)

Abbreviations: HIV, human immunodeficiency virus; MTB/RIF, Mycobacterium tuberculosis/ rifampicin; TB, tuberculosis

Discussion

The success of the use of robotic technology, internet, tablets, cell phones with disease-specific applications, telehealth, remote ultrasound and liver scans, as well as integrated electronic public health information systems and rapid diagnostic testing, have demonstrated that electronic/digital technologies can improve access to health services for remote First Nations communities. The use of technology has improved access of professionals to timely health care information, and has the potential to improve diagnostics capacity in the neediest areas of Saskatchewan. It has already enhanced timely client care and access to a wide variety of medical expertise in remote northern communities. These technologies have also increased the uptake of treatment and preventative measures such as vaccination and increased access to critical services (5,6,9,11,12,15,16). Technology use in health services have also proven to be cost-effective (2,5,6,9,16).

The increased use of health care technologies in remote northern communities in Saskatchewan has been positively received by patients. These technologies have resulted in increased patient comfort, as they avoid unnecessary transportation, and mean that people can stay with their families in their communities. In addition, through the use of these technologies, people have been empowered to help take care of their own health.

Although these technologies have helped to fill some of the existing gaps in the primary care to First Nations jurisdictions, there are some limitations that need to be considered: the use of technology can never completely replace the benefits of a direct or in-person encounter between a patient and a health care provider (14); technology can be resource intensive; and it requires training (11,16). To integrate the use of technology requires time and effort, and this integration involves extensive consultations with First Nations communities, local health care providers and First Nations leadership, as well as with representatives from various levels of government (5,6,11,16). Finally, technologies are not a panacea for some of the determinants of health that can affect the incidence and severity of infectious diseases in First Nations communities; however, their use does appear to address some of the geographic challenges that must be faced in providing health services to remote communities.

Because these are only preliminary findings, a formal and systematic evaluation of current practices would be of great value for future expansion of the use of these technologies. It would also be worthwhile to explore how these practices, and the lessons learned from these pilot projects, can be used in other areas to fill the gaps in services and improve health outcomes in the long term.

Conclusion

Currently, an increasing numbers of physicians and other health care professionals across Saskatchewan are using innovative technologies to improve access to health services. While gaps still exist, and more research is needed, the use of these technologies appears to be a safe, effective and cost-effective way to improve health care to remote First Nations and other communities.

Authors' statement

IK - conceptualization, investigation, writing original draft, methodology, software, validation, review and editing; KS, ND, VM - knowledge-sharing, review and editing

Conflict of interest

IK, NN, VM and IM have no conflict of interest to declare.

KS is a consultant and adviser to Gilead Sciences, AbbVie, Merck and has received grants from Gilead, AbbVie, Merck, Roche, Vertex Pharmaceuticals and ViiV Healthcare, but has no investments in any companies involved in pharmaceuticals or health care.

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Outbreaks in the age of syndemics: New insights for improving Indigenous health

A Andermann[1,2,3]*

Abstract

Conventional approaches for the prevention and control of communicable diseases within Indigenous contexts may benefit from new insights arising from the growing interest in syndemics. Syndemics is a term used to describe a conceptual framework for understanding diseases or health conditions, and how these are exacerbated by the social, economic, environmental and political milieu in which a population is immersed. The use of conventional approaches for outbreak prevention and control remains the bedrock of intervention in the field of communicable diseases; yet on their own, these strategies are not always successful, especially within contexts of marginalization and disadvantage. A broader approach is needed; one that examines the systemic factors involved, understands how various policies and systems support or hinder effective responses and identifies the structural changes needed to create more supportive environments and increase the resilience of the population. In an Indigenous context, whether the focus is on hepatitis C, tuberculosis, HIV or water-borne diseases, it is important to recognize that a) social determinants contribute to the emergence and persistence of outbreaks, b) conventional approaches to communicable disease control are necessary but not sufficient, and c) using a "syndemics lens" can leverage action at multiple levels to tackle the root causes of poor health and inform more effective strategies for improving Indigenous health and reducing health inequities.

Affiliations

[1] First Nations and Inuit Health Branch, Health Canada, Montréal, QC

[2] Department of Family Medicine, Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montréal, QC

[3] Department of Public Health, Cree Board of Health and Social Services of James Bay, Montréal, QC

Correspondence: anne.andermann@mail.mcgill.ca

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Introduction

There is a growing consensus in Canada that we need to improve the state of Indigenous health. It is well-known that, on average, Indigenous persons have a shorter life expectancy and shoulder a greater burden of chronic diseases. Communicable diseases also disproportionately affect Indigenous Canadians; for instance, the Indigenous population accounts for about 4.3% of Canada's total population but 17% of the tuberculosis burden, and newly-diagnosed infections among the Inuit are 270 times more likely than among Canadian-born non-Indigenous persons (1). Several factors are believed to contribute to this discrepancy, including historical factors, overcrowded living conditions and health system-related challenges. As well, the concurrence of health conditions such as HIV, diabetes and substance use increases the likelihood that latent tuberculosis infection will progress to active disease (2).

Recently, there has been a growing interest in the concept of syndemics within the global public health community. Syndemics is a term used to describe a conceptual framework for understanding diseases or health conditions, and how these are exacerbated by the social, economic, environmental and political milieu in which a population is immersed. This notion describes how co-existing health conditions can negatively reinforce each other and lead to worsening outcomes and greater vulnerability within the context of marginalization and disadvantage (3). Rethinking current strategies for communicable disease prevention and control in an Indigenous context would certainly benefit from a "syndemics lens" to guide responses that go beyond conventional approaches (i.e., vaccination and contact tracing), to include policies and programs that address the underlying and often structural root causes.

The concept of syndemics is closely linked to health equity and social determinants of health (4). The World Health Organization defines social determinants as "the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life" (5), such as economic policies, social norms and political systems. Those living in conditions of disadvantage are often more exposed to and less able to protect themselves from external threats to health and therefore suffer worse health outcomes. For example, a multi-cohort study and meta-analysis published recently in *The Lancet* followed over 1.7 million patients for an average of 13 years and found that participants aged 40-85 years with a lower socio-economic status had approximately 40% higher premature mortality and died on average two years earlier than those with a higher socio-economic status (6).

Social determinants of health include wide-ranging factors such as income, social support, early childhood development, education, employment, housing and gender (7). In an Indigenous context, extending beyond these social explanatory factors, there are even more deeply-embedded factors such as the history of colonization, jurisdictional ambiguity, structural

racism, intergenerational trauma and even the right to land ownership and enfranchisement, all of which can exert an important influence on population health, often in insidious ways (8). Indeed, there exist many frameworks that attempt to explain what social determinants are, how these factors interact and impact health, as well as ways to take action to reduce health inequities (9). In relation to Indigenous health, one of the most commonly used frameworks is the *First Nations Holistic Policy and Planning Model* developed by the Assembly of First Nations (10). This model highlights the importance of self-government and cultural continuity described by Chandler and Lalonde as underpinning determinants of resilience and well-being (11). A strong community is at the core of good health, and relationships (within communities, between communities and with formal institutions) are emphasized as key to building social capital (12). In this model, the holistic influence of the Medicine Wheel is prominent (i.e., focus on physical, mental, emotional and spiritual health), as well as the consideration of health across the entire lifespan (i.e., children, youth, adults and Elders).

While intuitively one might recognize that broader factors are at play, concretely there is the question of how can this new syndemics lens translate into a reduction in communicable disease morbidity and mortality? The purpose of this article is to explore how applying a syndemics lens can be useful in advancing infectious disease prevention and control among Indigenous populations in Canada.

Analysis

The case for the usefulness of a syndemics lens in strengthening infectious disease prevention and control in Indigenous contexts rests on three basic assertions: Social determinants of health are important contributors to the emergence and persistence of outbreaks; a number of infectious disease threats will not be optimally controlled unless social determinants of health are addressed; and using a syndemics lens can help inform novel approaches in clinical care, population health and public policy that can promote Indigenous health and reduce inequities.

Social determinants contribute to outbreaks

It is increasingly recognized that "poverty, overcrowding, population displacement, weak health systems, inadequate access to safe water and sanitation and the health status of specific populations are all contributing factors to epidemics and emerging disease outbreaks" (13). Those who live in degraded physical and social environments are at greater risk of contracting, propagating and even dying from communicable diseases (14).

This also holds true for Indigenous populations where it has been shown that "living in a house in need of major repairs, having less than high school education, being unemployed... experiencing food insecurity in the previous 12 months... and having no one to turn to for support in a time of need" are associated with negative health outcomes (15). It is well-documented that the living conditions of many Indigenous Canadians are considerably more precarious than their non-Indigenous counterparts. In 2011, "28% of on-reserve First Nations people and 30% of Inuit in Canada lived in crowded homes" as compared with 4% of non-Indigenous Canadians (16). Similarly, among Indigenous adults aged 25 to 64 years, "28.9% had no certificate, diploma or degree" while the proportion for non-Indigenous adults was 12.1% (17). Off-reserve, "approximately one in five (20.9%) [Indigenous] households was food insecure, including 8.4% with severe food insecurity", which is three times higher than non-Indigenous households where 7.2% were food insecure, including 2.5% with severe food insecurity (18).

There is a clear correlation between these living conditions and the higher rates of communicable diseases such as tuberculosis, community-acquired methicillin-resistant Staphylococcus aureus (MRSA) and sexually transmitted and blood-borne infections (STBBI) among Indigenous Canadians as compared with non-Indigenous Canadians (19). Indeed, there is a large body of literature linking higher rates of HIV among Indigenous populations to factors such as violence, stigma and discrimination, coupled with mistrust of the health system, "which contributes to poor HIV and health outcomes among Indigenous peoples" (19). An example of this is the recent outbreak of HIV among Indigenous peoples in Saskatchewan, with incidence rates 11 times the national average (20). Developing effective responses and models of care requires multi-faceted approaches to address the various aspects involved (21); such as considering the context of traumatic life experiences (22), including sexual abuse (23), as well as managing comorbidities including other sexually transmitted infections such as chlamydia, which is "estimated to be almost seven times higher among First Nations adults than the rate of the overall population" (24). It is possible to create culturally adapted approaches to address HIV outbreaks in Indigenous populations whereby 90% of people living with HIV know their status, are treated and achieve viral suppression. According to one Chief "Communication and confidentiality are key" (25).

Yet a recent report entitled *First Peoples, Second Class Treatment* describes the structural barriers that many Indigenous peoples continue to struggle with on a daily basis in obtaining access to quality care (26). Other structural barriers exist for a range of basic needs such as access to food, quality housing and clean water. The chronic challenge in accessing clean water on reserves, and the media attention this has received (27), led some people to use alternate unsafe water sources, resulting in water-borne illnesses (28). This complex situation of multiple co-existing epidemics represents a true syndemic, where the "compounding effects of multiple points of social disadvantage yield increasingly negative life outcomes" (15). In addition to vertical programs (i.e., single-disease approaches to communicable disease prevention and control), addressing the interconnected web of health and social challenges would benefit from greater emphasis on "person-centred" and systems-based approaches.

Conventional approaches are necessary but not sufficient

There is no question that conventional approaches to outbreak response (e.g., contact tracing and treating infectious cases) and promotion of preventive practices (e.g., hand hygiene, vaccination and safer sexual practices) are still the bedrock of communicable disease prevention and control measures (29). Yet, to make an impact on reducing disease incidence and

mortality, additional tools are needed to better understand and act, not only on health system factors, but also on the wider social, economic and political systems in place (30). It has long been recognized that "working and networking diligently with colleagues and appropriately communicating ideas and information across jurisdictional lines and between scientific disciplines are key to the success" of outbreak prevention and response (29).

With the rise in international travel and the interconnectedness of our global society, broader approaches that consider geopolitical concerns and shifting policy agendas are increasingly important for ensuring national and global health security (31). It has been argued that, in spite of the 2005 revision of the *International Health Regulations*, preventing public health emergencies of international concern (such as Ebola and Zika) will require stronger investment in health systems, particularly in low- and middle-income countries (32). The rise of antimicrobial resistance has become a United Nations (UN) priority in recent months, emphasizing the need for a unified and global approach to reducing communicable disease threats to health (33). Increasingly, it is clear that prevention cannot simply be transferred to the individual, with messages such as "wash your hands", "wear condoms" and "don't share needles", since individual behavioural change is only one piece of a much larger puzzle.

Indeed, missed opportunities for prevention and inequitable access to care have been identified as major factors in explaining health system inefficiencies (34), and ultimately poorer health outcomes. Health care system leaders are increasingly recognizing the need for a social determinants and population health approach not only for improving health, but also in balancing budgets, by "reducing healthcare demand and contributing to health system sustainability" (35). The health sector can play an important leadership role in addressing health inequities by making action on social determinants a health sector priority, and by integrating disparities reduction into policies, health programs and services (36).

In the realm of Indigenous health, the calls to action of the Truth and Reconciliation Commission (TRC) can serve as an important starting point and driver for making this happen (37). The TRC proposes to "fully adopt and implement the United Nations Declaration on the Rights of Indigenous Peoples as the framework for reconciliation," which states that "Indigenous peoples are equal to all other peoples... while recognizing the right of all peoples to be different, to consider themselves different, and to be respected as such" (38). Both the TRC calls to action and the UN declaration highlight the need to promote greater Indigenous self-determination, child welfare, economic development, justice, culture, language and education, which are all important social determinants of health. In particular, the TRC calls for action to "identify and close the gaps in health outcomes between Aboriginal and non-Aboriginal communities... including infant mortality, maternal health, suicide, mental health, addictions, life expectancy, birth rates, infant and child health issues, chronic diseases, illness and injury incidence, and the availability of appropriate health services." Since the role of the health sector is to improve health (not only to create health services) (39), action on social determinants falls squarely within this mandate. Moreover, the tools to achieve these goals are within reach when one adopts a syndemics lens.

A syndemics-informed approach can address the root causes

Effective strategies for addressing the social determinants of health have been developed in recent decades for frontline health workers in busy clinical settings (40), for public health professionals working at a population level (41) and even for decision-makers at a public policy level (42). The following analysis explores how some of these best practices can be applied to addressing syndemics, with the aim of improving overall health and reducing inequities among Indigenous populations.

Clinical best practices to address syndemics among Indigenous peoples

There are now well-articulated best practices for taking action on the social determinants of health in clinical practice; at a patient care level, at a practice level and at a community level (**Table 1**). These can be applied as useful complements to conventional strategies for preventing and managing communicable diseases in Indigenous populations.

Table 1: A dozen best practices to address syndemics in clinical practice[1]

Approach	Best practices
At the patient care level	Treat patients with dignity and respect and create a safe space for disclosure Ask patients about social challenges in a sensitive and caring way Allocate a little extra time to address complex health and social needs Know about local referral resources Refer patients and help them access benefits and support services
At the clinic or nursing station level	Consider adding chart reminders or recall systems to flag patients at risk Consider participatory approaches that engage other clinicians in your practice to create a culture of reflection and a more "upstream approach" Consider alternative models of care such as outreach, or using patient navigators to assist patients on their journey through the health and social systems
At the community level	Reach out to local leaders to discuss the health and social challenges that are common in the community Use clinical experience and research evidence to advocate for social change Get involved in community needs assessment and health planning Partner with community groups, public health and local leaders to advance collaborative initiatives that help address or attenuate the effects of health inequities

[1] Summarized from (40)

For example, a nurse working in a remote Indigenous community may become aware that sexually-transmitted infections are very common in the local population, particularly among youth. She notes that few youth spontaneously come to the nursing station unless they have had an acute injury or other emergency requiring immediate care. The nurse, therefore, tries a different approach to develop a relationship of trust with the young people in the community by organizing a weekly "coffee house" and movie night. These become very popular and gradually young people open up about their concerns and the nurse is able to advise them on issues such as healthy relationships, family planning, alcohol and drug use and violence prevention. Over time, more young people visit the clinic to receive sexual health counselling and screening for infectious diseases, as well as treatment and referral for various health and social services. Once the nurse has a deeper understanding of the key challenges and dynamics in the local context, she starts to think about what could be done at the community level to create more supportive environments for health, and initiates a dialogue with the Youth Council leader, the school principal, Elders, natural helpers and other community members, and this leads to a Youth Health gathering to discuss the way forward for creating wider community-level change. Though there are no "one size fits all" solutions, health workers at the frontlines can be important catalysts for taking action on the social determinants of health at multiple levels.

Public health and policy approaches to syndemics in Indigenous populations

In addition to implementing the action areas of the Ottawa Charter for Health Promotion (43), building healthy public policies and creating supportive environments for health, more recent efforts to reduce health inequities have focused primarily on intersectoral action and a "health in all policies" (HiAP) approach. Intersectoral action involves the collaboration of multiple sectors, such as education, justice and employment in addressing complex challenges. The HiAP approach refers to the involvement and support of all levels of government with strong leadership at the highest levels (44). Increasingly, there are examples of best practices, even within a communicable disease context, on how to create structural change through establishing policy goals, building capacity, fostering multi-level partnerships across sectors and holding leadership accountable for real change (45).

A key element in intersectoral work and the HiAP approach is the engagement and meaningful involvement of those who will most be affected by the decisions being made. Whether at a population or a political level, ethical choices not only involve ensuring that the overall benefits outweigh the harms, and that the distribution of benefits and harms are fair (46), but that there is a fair and transparent process for making such decisions (47). The engagement of Indigenous peoples in decisions that affect their health requires an ongoing process to "create opportunities for community voice and action to affect social and structural conditions that are known to have wide-ranging health effects on communities" (48). In every aspect of decision-making that impacts people's daily lives, Indigenous peoples should be involved in the decision-making process. According to the UN Declaration on the Rights of Indigenous Peoples: "Indigenous peoples have the right to participate in decision-making in matters which would affect their rights, through representatives chosen by themselves in accordance with their own procedures, as well as to maintain and develop their own Indigenous decision-making institutions" (38). There is a saying, that even with the best intentions, there should be "Nothing about us without us." It is the involvement, empowerment and self-determination in shaping and defining solutions to complex problems that are in themselves important outcomes (i.e. a fair and transparent process is part of the solution).

Compared to the clinical arena, decisions made at the population and public policy levels are more complex and include a much larger number of players (49). Particularly when dealing with areas of shared jurisdiction (which is very common when addressing issues relating to Indigenous health) (50), it is important to have the many different partners working together towards a shared goal of better health and reduced inequities. There are limited examples in the published literature of such intersectoral action as it relates to improving the health of Indigenous Canadians (51), but it is starting, and needs to become part of the modus operandi before progress can be made in reducing inequities in Indigenous health.

In addition to formalized tri-partite structures (involving federal, provincial and Indigenous government representation; such as the BC First Nations Health Authority and the Manitoba Inter-Governmental Committee on First Nations Health) (52), which are increasingly being used, there are many ways to develop intersectoral and multi-institution partnerships to overcome areas of jurisdictional ambiguity. For instance, preventing water-borne communicable diseases on reserves is an important challenge, which requires the collaboration of many different individuals and organizations. Legislation governing access to clean water is not without its shortcomings (53). The Walkerton crisis has taught us that even in non-Indigenous settings, breakdowns in water-monitoring and communication can lead to outbreaks of water-borne illness and even deaths, all of which are potentially avoidable. The Walkerton inquiry highlighted the importance of routine testing of water, logging of results and rapid communication of abnormal results with public health officials to ensure appropriate preventive action (e.g., drinking water advisories and ensuring adequate water treatment systems) (54). This is part of a multi-barrier approach to protecting citizens from harm, which is also relevant to Indigenous settings (55).

When developing mechanisms to protect Indigenous peoples from water-borne illness, it is important to have Indigenous and other partners at the same table (or on the same teleconference call) to sort out the details of how to make it work "on the ground." Convening the Regional Medical Officer and the Regional Manager of the Environmental Health Program of the First Nations Inuit Health Branch at Health Canada, the Director of Infrastructure and Housing at the Regional Office of Indigenous and Northern Affairs Canada, the team at the provincial Ministry of Environment responsible for enforcement of provincial water regulations, the person working under the Chief Medical Officer of Health at the provincial Ministry of Health with delegated responsibility for Environmental Health Protection and, of course, representatives from Indigenous communities and/or Indigenous governance organizations—all of whom can then work together, as a necessary first step to develop a shared understanding of the complexities involved

and to propose strategies to facilitate communication and transparency in achieving shared goals.

This collaborative approach to working through these complexities can help ensure that there is no appearance of a "double standard" when it comes to how water quality is managed on- and off-reserve. If certain municipalities are granted exemptions (e.g., not required to ship the requisite number of water samples each month to the accredited laboratories due to remote location and transportation challenges), then there can be similar allowances for Indigenous communities with the same distance barriers; but the regulations should be applied in a similar manner, regardless of ethnicity and cultural background of inhabitants. If water processing plants need to meet certain accreditation standards or community-based water-monitors must possess specific training certifications recognized by regulation authorities, then these are all specific objectives that should be worked towards to ensure that all peoples are equally protected under the law. In this way, it will be possible to overcome the many structural and organizational barriers to population and policy-level change, including "limited time or resources, inflexible policies, insufficient managerial support and departmental silos" (56). It may not be a quick fix, but moving forward together is likely to identify more effective and sustainable solutions to complex challenges and certainly a more inclusive and fair process. Indeed, there are examples from other jurisdictions of how Indigenous voices have been used in decision-making processes, and these examples can be used as further inspiration (57).

With climate change ushering in a northward progression of communicable disease vectors, such as ticks carrying Lyme disease to Canada, traditional ways of knowing and the wisdom of Elders can be very helpful. There is an Indigenous saying: "We do not inherit the earth from our parents, but borrow it from our children." (58) This points to the wisdom of decision-making that considers the impact on future generations. We have a great deal to learn from Indigenous approaches to health and well-being, not only for our own health, but also for the health of animals, the land and fulfilling our custodial responsibility towards the well-being of our planet (59,60).

Conclusion

Conventional approaches to communicable disease prevention and control are no longer sufficient in addressing some of the serious infectious disease threats, both in Canada and around the world. While there is increasing interest within the medical and public health communities regarding the importance of a social determinants approach, the conversation on health inequity in Canada has only recently gained traction. We still have a lot to learn about how to assess these inequities and how to better work together, across departments and sectors, to find effective solutions for health and social challenges.

The Truth and Reconciliation Commission highlights the need for greater involvement of Indigenous peoples in creating their own systems, structures and futures. Using a syndemics lens and taking a social determinants approach can help to better appreciate and act on the root causes of poor health as a means of reducing susceptibility and increasing the resilience of all Canadians, including Canada's Indigenous peoples. As this is an emerging area of action, we need to report on and share best practices and success stories – whether at the clinical, population health or public policy levels – to advance our work together towards creating a healthier, more equitable and sustainable society.

Authors' statement

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Conflict of interest

None.

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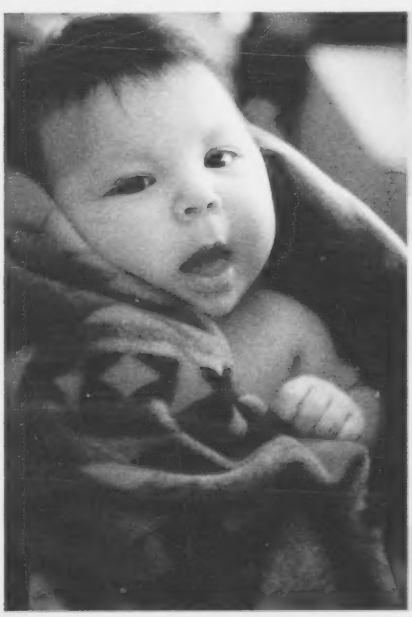

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Cox AD, Barreto L, Ulanova M, Bruce MG, Tsang RSW on behalf of the Conference contributors. Developing a vaccine for Haemophilus influenzae serotype a: Proceedings of a workshop. Can Commun Dis Rep. 2017;43(5):89-95.

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Evaluating the timeliness of reporting in a First Nations communicable diseases program

A Lam[1,2]*, S Woods[3], N Ndubuka[2]

Affiliations

[1] Canadian Public Health Service, Public Health Agency of Canada, Ottawa, ON (at the time of study)

[2] Northern Inter-Tribal Health Authority, Prince Albert, SK

[3] Prince Albert Grand Council, Prince Albert, SK

Correspondence: andrew_lam@rocketmail.com

Abstract

Background: Timely reporting of communicable diseases is necessary to enable a prompt response to mitigate and control outbreaks. This is especially true among First Nations communities due to a number of factors, including unique social determinants of health, which can contribute to rapid disease transmission.

Objective: To assess the timeliness of reporting for 12 notifiable communicable diseases in the Northern Inter-Tribal Health Authority, which includes 33 First Nations on-reserve communities in Northern Saskatchewan, Canada, and to assess whether there were differences in reporting times depending on degree of remoteness of community, season or year.

Methods: Data for four sexually transmitted infections (STIs) and eight other communicable diseases were abstracted from the integrated Public Health Information System (iPHIS) between 2008 and 2013 and compared against the targets set for reporting in the Saskatchewan Communicable Disease Control Manual. The reporting time was defined as the duration from client exposure or presentation at clinic to the case notification day at Saskatchewan's Ministry of Health. Communicable diseases were evaluated for proportion of cases reported within recommended time, and mean reporting time. Geographical and reporting data were also recorded to assess variations in reporting time among different northern communities and according to season or year.

Results: A total of 9,767 records were identified for the 12 diseases; all had a 14-day recommended reporting time, with the exception of shigellosis, which had a three-day reporting time. Overall, 93.6% of the diseases were reported in the recommended reporting time, although there was variability among the diseases. All four of the STIs (chlamydia, gonococcal infections, HIV and syphilis) had over 90% of cases reported within the 14-day recommended time period. Other communicable diseases reporting times varied from a high of 93.4% for methicillin-resistant *Staphylococcus aureus* (MRSA), 91.7% for lab-confirmed influenza and 89.1% for streptococcal A-invasive disease to a low of 16.2% for shigellosis and 12.2% for pertussis. Salmonellosis and pneumococcal-invasive disease were intermediary with 77.4% and 72.2%, respectively. Mean reporting times indicated that eight of the 12 diseases (66.7%) had reporting times similar to or better than recommended times. There appeared to be a correlation between longer reporting periods and the more northern communities. There were no seasonal variations found but yearly-trend analysis demonstrated an anomalous year in 2011, in which all communicable diseases with the exception of STIs experienced a peak in reporting delays.

Conclusion: Overall, communicable disease reporting in this northern health authority program met recommended reporting times, although there were variations according to the disease, the area reporting and the year. Further research is needed to understand these variations in order to inform efforts to strengthen communicable disease surveillance among First Nations communities.

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Introduction

The purpose of a surveillance system is to monitor events and enable a response from public health and front line clinical care (1,2). In a communicable disease (CD) surveillance system, the timeliness of response to CD events is essential in order to attenuate the spread of a disease and prevent an outbreak occurrence. Timeliness is a key attribute recommended in the evaluation of surveillance systems by both the Centres for Disease Control and Prevention and the World Health Organization (3-5). Many studies have evaluated the timeliness of national CD surveillance systems (6-9); however, limited information from evaluations of regional CD surveillance systems have been published.

It is well-known that Indigenous peoples in Canada have a disproportionate amount of the infectious disease burden (10,11). These higher incidence rates are attributable to social determinants of health such as overcrowding, lack of access to health care services and lower education (12,13); however, to understand and appropriately respond to the burden of infectious diseases, it is important to ensure adequate monitoring of this information. Yet, to our knowledge, very

little has been published on CD surveillance systems among Indigenous peoples in Canada.

The Northern Inter-Tribal Health Authority

The Northern Inter-Tribal Health Authority (NITHA) is a regional First Nations health organization that comprises four partners: Meadow Lake Tribal Council; Lac La Ronge Indian Band; Prince Albert Grand Council; and Peter Ballantyne Cree Nation. NITHA's public health unit conducts CD surveillance for over 32,000 Registered Indians among Northern Saskatchewan's 33 First Nations on-reserve communities. These communities are distributed among six Regional Health Authorities across Northern Saskatchewan. The CD program at NITHA reports data and conducts follow-up investigations in adherence to *The Public Health Act, 1994*, the Saskatchewan *Disease Control Amendment Regulations*, 2014 and the Saskatchewan Ministry of Health's *Communicable Disease Control Manual* (14,15). At NITHA, all notifiable CDs, with the exception of tuberculosis, are monitored within the CD program. The higher prevalence of tuberculosis among First Nations communities warranted a separate TB program at NITHA for its investigation.

Clinicians, within communities or off-reserve, collect and submit specimens to the *Saskatchewan Disease Control Laboratory* (SDCL) for laboratory confirmation of the CD. Laboratory results are sent to the Regional Health Authorities, which send the results to the specific regional health organizations. So if the client is a resident from a community within NITHA's coverage, the results would be sent to NITHA. NITHA is then responsible for connecting with frontline community health staff for client follow-up. NITHA reports both laboratory and follow-up information to Saskatchewan's Population Health Branch using the integrated Public Health Information System (iPHIS).

In light of the disproportionate CD burden among First Nations communities, and the lack of research evaluating regional CD surveillance, the objective of this study was to identify the timeliness of CD reporting by NITHA to Saskatchewan's Population Health Branch and assess whether there were differences in reporting times by remoteness of community, season or year.

Methods

Data Collection

Data for sexually transmitted infections (STIs) and other CDs were collected from iPHIS for a six-year time period between January 1, 2008 and December 31, 2013. Twelve diseases had a sufficient number of cases over the six year data collection period for disease-specific analysis in this study. Those twelve diseases included four STIs: *Chlamydia trachomatis*; gonococcal infections; human immunodeficiency virus (HIV); and syphilis; and eight other CDs: hepatitis C; influenza; methicillin-resistant *Staphylococcus aureus* (MRSA); pertussis; pneumococcal-invasive disease; salmonellosis; shigellosis; and streptococcal A–invasive disease.

Reporting time

Line listing data from iPHIS for the CDs under study included two dates for each CD: episode date and diagnosis date for STIs; and episode date and laboratory reported date for the other CDs. Reporting time was defined as the number of days from the episode/encounter in the clinic to the diagnosis/laboratory-reported date. This interval indicated the duration of time between the client presentation at the health facilities, where the specimen was collected, and the time when the result was reported by NITHA to Saskatchewan's Population Health Branch through iPHIS.

Geography and trends over time

Line listing data from iPHIS included names of 33 First Nations on-reserve communities in Northern Saskatchewan, Canada. The communities were clustered into five councils and geographical areas for analysis: Prince Albert Grand Council; Meadow Lake Tribal Council; Peter Ballantyne Cree Nation; Lac La Ronge Indian Band; and the most northern NITHA communities. Trends over time by season and year were assessed by assigning the season or year of the case by the episode/encounter date.

Statistical analysis

The comparator to assess the reporting time was the Saskatchewan CD Control Manual recommended time limit for each of the 12 CDs (16); all had a 14-day recommended reporting time, with the exception of shigellosis that had a three day reporting time. Timeliness was analyzed by calculating: a) the proportion of cases that were reported within the recommended time limit; and b) the mean reporting time between the two dates. Confidence intervals with an alpha of 0.05 were calculated, where available. Analyses were performed using Microsoft Office Excel 2010 and statistical software R (17). Only diseases that had more than 30 cases during the observed time period were included in the disease-specific analyses. Yearly reporting time trend analyses were conducted for the total group of STIs and other CDs to account for sample size limitations of individual disease analyses.

Results

Among the twelve diseases, a total of 9,767 records were identified and 93.6% of the diseases were reported in the recommended reporting time (**Table 1**). *C. trachomatis*, MRSA, and gonococcal infections were the most prevalent diseases, constituting 51.1%, 23.2% and 16.8% of the identified cases respectively. All STIs (chlamydia, gonococcal infections, HIV and syphilis) had over 90% of cases reported within the recommended time period; *C. trachomatis* was reported on time for 96.9% of cases, HIV for 97.5% of cases, gonococcal infections for 95.8% of cases and syphilis for 90.7% of cases. MRSA and lab-confirmed influenza also had a high proportion of cases reported on time: 93.4% and 91.7%, respectively. The two CDs with the lowest proportion of cases reported on time were pertussis, at 12.2%, and shigellosis, at 16.2% (shigellosis was the only CD with a recommended three day reporting period).

The remaining CDs were reported on time for 70-90% of cases; these included hepatitis C, pneumococcal-invasive disease, salmonellosis and streptococcal A-invasive disease.

Table 1: Number and percent of common communicable diseases from the Northern Inter-Tribal Health Authority reported within the recommended time, 2008–2013[1]

Type of infection	Name of infection	Number of records (% of total)	Number within the recommended reporting time (%)[1]
Sexually transmitted infections	*Chlamydia trachomatis*	4, 989 (51.1)	4,835 (96.9)
	Gonococcal infections	1,636 (16.8)	1,567 (95.8)
	HIV	80 (0.8)	78 (97.5)
	Syphilis	43 (0.4)	39 (90.7)
Other communicable diseases	Hepatitis C	262 (2.7)	212 (80.9)
	Influenza (lab-confirmed)	229 (2.3)	210 (91.7)
	MRSA	2,265 (23.2)	2,115 (93.4)
	Pertussis	82 (0.8)	10 (12.2)
	Pneumococcal-invasive disease	36 (0.4)	26 (72.2)
	Salmonellosis	31 (0.3)	24 (77.4)
	Shigellosis	68 (0.7)	11 (16.2)
	Streptococcal A-invasive	46 (0.5)	41 (89.1)
Combined	Total	9,767	9,141 (93.6)

Abbreviations: HIV, Human Immunodeficiency Virus; MRSA, Methicillin-Resistant Staphylococcus aureus, %; percent

[1] Recommended reporting time was based on targets noted in the Saskatchewan CD Control Manual-14 days for all CDs with the exception of shigelloisis, which was three reporting days

Mean reporting time

Most CDs had significantly shorter mean reporting times compared with recommended times (**Table 2**). Syphilis had the longest mean reporting time of 21.1 days; however, reporting times for syphilis, hepatitis C and pneumococcal-invasive disease were not significantly different from recommended times. Shigellosis was the only disease that had a mean reporting time significantly greater than the recommended time at 13.6 days versus three days. Shigellosis was also the only disease with a median reporting time outside the recommended time (*data not shown*).

Table 2: Mean reporting time from the Northern Inter-Tribal Health Authority to the Saskatchewan Population Health Branch of common infectious disease, 2008–2013

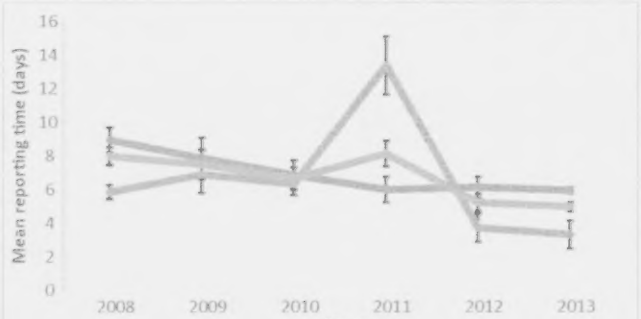
Type of infection	Name of infection	Mean reporting time in days (95% CI)
Sexually transmitted infections	*Chlamydia trachomatis*	7.1 (6.5, 7.6)
	Gonococcal infections	7.9 (7.1, 8.7)
	HIV	8.2 (7.0, 9.4)
	Syphilis	21.1 (0.7, 41.5)
Other communicable diseases	Hepatitis C	15.1 (5.9, 24.3)
	Influenza (lab-confirmed)	7.3 (4.8, 9.8)
	MRSA	5.7 (5.2, 6.2)
	Pertussis	8.5 (6.4, 10.7)
	Pneumococcal invasive disease	10.6 (5.5, 15.8)
	Salmonellosis	9.9 (7.2, 12.7)
	Shigellosis	13.6 (9.2, 17.9)
	Streptococcal A-invasive	6.1 (2.9, 9.3)

Abbreviations: CI, confidence intervals; HIV, Human Immunodeficiency Virus; MRSA, Methicillin-Resistant *Staphylococcus aureus*; %, percent

Trends over time

The annual mean reporting times of STIs and other CDs were evaluated to observe annual trends (**Figure 1**). STIs had a recommended reporting time of 14 days, and were consistently reported to the Saskatchewan Population Health Branch in fewer than 10 days. Between 2008 and 2013, there was a downward trend in reporting timeliness for STIs. The reporting of other CDs was within the recommended time, with the exception of the year 2011, when cases took an average 11.7-15.2 days (95% confidence interval) to be reported. The overall trends for both groups of other CDs and of all CDs combined were downward sloping between 2008 and 2013, as was seen with STIs.

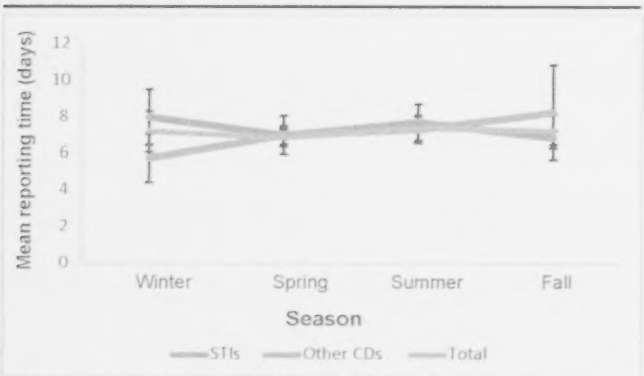
Figure 1: Mean reporting times for different communicable diseases between 2008 and 2013



Abbreviations: STIs, sexually-transmitted infections; CDs, communicable diseases
Figure note: Error bars depicting a 95% confidence interval are shown

Data for STIs and other CDs from each of the four seasons were analyzed to observe seasonal trends. There were no differences of mean reporting times between or within any group of CDs throughout the four seasons (**Figure 2**).

Figure 2: Mean reporting times for different communicable diseases during the different seasons



Abbreviations: STIs, sexually-transmitted infections; CDs, communicable diseases
Figure note: Error bars depicting a 95% confidence interval are shown

Mean reporting times for communities and councils were also evaluated from collected data. Mean reporting times were significantly less for Meadow Lake Tribal Council and Peter Ballantyne Cree Nation compared with the northernmost communities. Reporting times from Lac La Ronge Indian Band and Prince Albert Grand Council did not differ between the other communities (*data not shown*). Data suggests longer reporting times were associated with remoteness of the communities.

Discussion

Based on almost 10,000 records from First Nations communities over a six-year period, NITHA was successful in reporting 93.6% of common CDs within the recommended reporting time, although there was some variation among the different diseases. Pertussis and shigellosis were reported least frequently within the recommended time. Pertussis and shigellosis may have had delayed reporting due to clusters and outbreaks of these two diseases, which strained public health resources and prolonged reporting (18). The relatively small number of records for these two diseases also implies that a delay of a few cases can drastically reduce the proportion of timely reported incidents. There was no significant seasonal variation and reporting times were generally getting shorter over the time period of the study. One exception to this was the increased reporting times seen in 2011. This occurred at the time of a shigellosis outbreak, which may have strained public health capacity and created an overall delay in the CD program (19). In terms of geographical analysis, the northernmost communities had slightly longer reporting periods than those communities closer to Regina, Saskatchewan.

This study reports on one of the first evaluations of CD surveillance programs for First Nations communities recently published in the scientific literature. In addition, this was one of the first studies that analyzed both mean and median reporting times, while other studies measured only median reporting times (7,8,20). Measurement of both mean and median reporting times for Shigellosis helped to better understand the distribution of reporting times (8).

There are some limitations to the study. First, there were an insufficient number of records for many CDs. This uncontrollable phenomenon prevented meaningful statistical analyses from being conducted, such as evaluating disease-specific yearly trends. Additionally, data collected from iPHIS only displayed two unique dates for most entries. This system limitation prevented evaluation at individual steps of the surveillance program. For instance, other common steps to evaluate would have been time between exposure and diagnosis, time between patient encounter and laboratory confirmation and time between laboratory confirmation and reporting to the appropriate health unit (5,8). Finally, timeliness is just one aspect of evaluation of a surveillance system, and other indicators, such as internal completeness, internal and external validity and usefulness are other aspects that are often assessed (21).

In terms of next steps, this evaluation has shown that CD reporting does vary by disease, year and remoteness of the community. This evaluation does not explain why the variance occurs. Future investigations may help to explain this by analyzing with increased sample sizes or by conducting qualitative studies to understand reporting mechanisms; for example, the current system uses paper reporting forms whereas an electronic system may be beneficial in achieving a more consistent timely reporting rate (6). Finally, cumulative delay distribution graphs may also be valuable for future analyses (7).

Conclusion

The communicable disease program at NITHA successfully reported 93.6% of all collected communicable disease cases to the Saskatchewan Population Health Branch in a timely manner, although there were variations according to the disease, year and remoteness. The reporting times for specific diseases, such as shigellosis, syphilis, hepatitis C, and pneumococcal-invasive disease, could be improved to consistently achieve timely reporting.

Authors' statement

ATL – Conceptualization, methodology, analysis, writing – original draft, review and editing; SW – Conceptualization, writing – review and editing, and supervision; NN – Writing – review and editing, and supervision

The views expressed in this article are the authors' own and not an official position of any affiliated organization.

Conflict of Interest

None.

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ADVISORY COMMITTEE STATEMENT

Summary of the NACI Update on the recommended use of Human Papillomavirus (HPV) vaccine: Nine-valent HPV vaccine two-dose immunization schedule and the use of HPV vaccines in immunocompromised populations

SL Deeks[1,2], MC Tunis[3], S Ismail[3] on behalf of the National Advisory Committee on Immunization (NACI)*

Affiliations

[1] NACI HPV Working Group Chair, Toronto, ON

[2] Immunization and Vaccine Preventable Diseases, Public Health Ontario, Toronto, ON

[3] Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada, Ottawa, ON

***Correspondence:** naci-ccni@phac-aspc.gc.ca

Abstract

Background: Human papillomavirus (HPV) infections are the most common sexually transmitted infections. In the absence of vaccination, it is estimated that 75% of sexually active Canadians will have an HPV infection at some point in their lives. HPV vaccine programs were first recommended by Canada's National Advisory Committee on Immunization (NACI) in 2007. In addition to the existing HPV vaccine options in Canada, NACI recently recommended the use of a newly authorized nine-valent HPV (HPV9) vaccine according to a 3-dose immunization schedule for the prevention of HPV types 6-, 11-, 16-, 18-, 31-, 33-, 45-, 52- and 58-related cancers and anogenital warts in females aged 9 to 45 years and males aged 9 to 26 years. New data have emerged evaluating a 2-dose immunization schedule for HPV9 vaccine in males and females, which NACI reviewed in order to provide timely guidance on the possibility of a 2-dose immunization schedule for HPV9 vaccine. Recently, a growing number of studies have also specifically explored the responses of immunocompromised subgroups to HPV vaccines, which also triggered a NACI literature review and updated recommendations on this topic.

Objectives: To review evidence for a 2-dose immunization schedule of the HPV9 vaccine and provide recommendations on vaccine schedule; and to summarize evidence from a recent NACI literature review on the use of HPV vaccines in immunocompromised populations and provide recommendations for HPV vaccine use in these groups.

Methods: The NACI HPV Working Group reviewed results from a clinical trial of HPV9 vaccine administered with a 2-dose immunization schedule in males and females (protocol V503-010) and performed a literature review on the topic of HPV immunization of immunocompromised populations. The NACI literature review and the NACI statement were published separately.

Results: Only one study investigated a 2-dose immunization schedule with HPV9 vaccine, a large manufacturer-sponsored randomized controlled trial (protocol V503-010) of good quality. Taken in context of studies with other HPV vaccines, NACI considered this study to be a sufficient evidence base for recommendations. Through a comprehensive literature review, 27 studies were identified for evidence synthesis including reports on vaccine immunogenicity, safety, or both for immunocompromised populations.

Conclusions: Based on the evidence reviewed, NACI issued new recommendations for the use of HPV9 vaccine with a 2-dose immunization schedule at 0, 6-12 months in young females and males and updated the grade of evidence for the use of HPV vaccines in immunocompromised populations.

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Introduction

HPV infections are the most common sexually transmitted infections. In the absence of vaccination, it is estimated that 75% of sexually active Canadians will have a human papillomavirus (HPV) infection at some point in their lives. Quadrivalent (HPV4) and bivalent (HPV2) HPV vaccines have been authorized for use in Canada since 2006 and 2010, respectively. The National Advisory Committee on Immunization (NACI) has previously recommended HPV4 vaccination in males and females according to a 3-dose (0, 2, 6 months) or a 2-dose (0, 6 months) immunization schedule, or HPV2 vaccination for females according to a 3-dose (0, 1, 6 months) or a 2-dose (0, 6 months) immunization schedule, depending on the age and health status of the recipient. In February 2015, a nine-valent HPV vaccine (HPV9) (Gardasil®9, Merck Canada, Inc.) was authorized for use in Canada for the prevention of HPV types 6-, 11-, 16-, 18-, 31-, 33-, 45-, 52- and 58-related cancers and anogential warts in females aged 9 to 45 years and males aged 9 to 26 years; this vaccine was recommended by NACI as a 3-dose immunization schedule in a NACI Statement (1) and *Canada Communicable Disease Report* (CCDR) summary (2) published in July 2016. Immunization against HPV types 16 and 18 can prevent approximately 70% of anogenital cancers and 60% of high-risk precancerous cervical lesions. It is estimated that immunization against the additional five HPV types contained in the HPV9 vaccine can prevent up to an additional 14% of anogenital cancers and up to 30% of high-risk precancerous cervical lesions.

NACI reviewed new clinical trial evidence for a 2-dose immunization schedule of HPV9 vaccine in order to provide timely guidance on the possibility of a 2-dose immunization schedule for HPV9 vaccine. Previous NACI Statements have also discussed the use of HPV vaccines in immunocompromised populations, but this has been largely in the absence of strong evidence for these groups. Recently, a growing number of studies have specifically explored the responses of immunocompromised subgroups to HPV vaccines, which triggered a NACI Literature Review on this topic and advice in the statement. This paper summarizes the recent NACI Statement on the evidence and recommendations for a 2-dose immunization schedule for HPV9 vaccine (3) and the NACI Literature Review that updates the evidence on the use of HPV vaccines in immunocompromised persons (4). These new recommendations are published in the full NACI Statement (3) and also in the HPV chapter of the *Canadian Immunization Guide*, where all current HPV recommendations from NACI are synthesized and presented together (5).

Methods

NACI reviewed key questions on HPV9 vaccine as proposed by the HPV Working Group, including: the safety, immunogenicity and efficacy of the HPV9 vaccine with a 2-dose immunization schedule. Only one manufacturer-sponsored clinical trial was identified (protocol V503-010) (6). The NACI HPV Working Group reviewed detailed study methods and results obtained from the vaccine manufacturer. Two independent reviewers appraised the study for internal validity to assign the level and quality of evidence, which was validated by the Working Group Chair and subjected to a modified peer review process by the Working Group and NACI.

NACI also reviewed key questions for a literature review on HPV vaccines in immunocompromised populations as proposed by the HPV Working Group, including the specific question: "Do immunization outcomes differ for subgroups of immunocompromised populations?" A literature review was conducted according to established NACI methodology (7). Details of this literature review and associated methodology (search terms, inclusion/exclusion criteria, databases, number of results) can be found in the *NACI Literature Review for HPV Immunization of Immunocompromised Populations* (4). Proposed recommendations were developed based on the literature review. NACI approved specific evidence-based recommendations and elucidated the rationale and relevant considerations in the statement update.

Results

A large randomized controlled trial of good quality, demonstrating that immunogenicity following a 2-dose immunization schedule among females and males 9 to 14 years of age, was not inferior to a 3-dose schedule in women 16 to 26 years of age. Taken in context of studies on 2-dose immunization schedules with other HPV vaccines, NACI considered the body of evidence to be sufficient to issue recommendations on a 2-dose immunization schedule for HPV9 vaccine.

On the topic of immunocompromised populations, the literature review identified 27 studies for evidence synthesis including reports on immunogenicity, safety, or both (4). Studies were grouped broadly into two categories: HIV infected populations and groups receiving therapeutic immunosuppression. Cohort study was the predominant experimental design and most included a low participant number with quality ranging from good to poor.

Immunosuppressive regimes were typically reported for patients with acquired therapeutic immunodeficiency, but unfortunately these studies did not often stratify results according to treatment modality. The extent of effective immunosuppression was not measured or reported in any study, but CD4 counts were typically provided for studies of HIV infected patients. All studies used HPV2 or HPV4 vaccines with a routine 3-dose schedule, except one study which provided an additional fourth dose. No study used the recently-authorized HPV9 vaccine.

Conclusion

Based on the evidence reviewed, NACI issued three recommendations on the use of a 2-dose immunization schedule in immunocompetent populations and the use of HPV vaccines in immunocompromised populations (**Text box**).

RECOMMENDATIONS FOR 2-DOSE HPV9 SCHEDULE IN IMMUNOCOMPETENT POPULATIONS

Recommendation 1: Immunocompetent Females and Males 9-14 Years of Age

NACI recommends that HPV9 vaccine should be offered according to either a 2-dose or 3-dose immunization schedule in immunocompetent females and males 9 to 14 years of age (as with HPV2 or HPV4 vaccines in females, and HPV4 vaccine in males in this population) - NACI Evidence Grade B Recommendation (fair evidence to recommend immunization).

NACI concludes that there is now fair evidence to recommend a 2-dose immunization schedule with HPV9 vaccine, although evidence is limited in quantity. Therefore, based on the current evidence reviewed for this and previous Advisory Committee Statements, NACI concludes that there is fair evidence to recommend either a 2-dose or a 3-dose immunization schedule with HPV9 vaccine (Evidence Grade B) and that there is good evidence to recommend either a 2-dose or a 3-dose immunization schedule with HPV2 or HPV4 vaccines (in females) and HPV4 vaccine (in males). In a 2-dose HPV immunization schedule with any HPV vaccine authorized for use in Canada, the second dose should be administered at least 24 weeks (6 months) after the first dose. Although long-term follow-up data are not currently available for a 2-dose schedule with HPV9, a study is currently underway to evaluate the duration of vaccine responses up to 36 months. As further evidence becomes available, the grade of this recommendation may change. There is no evidence to suggest that individuals will respond differently to HPV9 vaccine compared to either HPV2 or HPV4 vaccines.

Recommendation 2: Immunocompetent Females and Males ≥15 Years of Age

NACI continues to recommend that HPV9 vaccine should be offered according to a 3-dose immunization schedule in immunocompetent females and males 15 years of age and older (as with HPV2 or HPV4 vaccines in females and HPV4 vaccine in males) - NACI Evidence Grade B Recommendation (fair evidence to recommend immunization).

There are currently no studies directly evaluating a 2-dose immunization schedule for HPV9 vaccine in males and females 15 years of age and older. Therefore, a 3-dose schedule continues to be recommended in these populations. This recommendation is outlined in the previous statement *Updated Recommendations on Human Papillomavirus (HPV) Vaccines: 9-valent HPV vaccine and clarification of minimum intervals between doses in the HPV immunization schedule*. However, a recent study in India has suggested that 2 doses of HPV4 vaccine may be immunogenic in females aged 10-18 years, and NACI will continue to review similar evidence as it emerges in order to identify the optimal HPV9 immunization schedule for persons 15 years of age and older.

RECOMMENDATIONS FOR HPV VACCINATION IN PERSONS WHO ARE IMMUNOCOMPROMISED AS A RESULT OF DISEASE OR MEDICATIONS

Recommendation 3:

NACI continues to recommend that HPV vaccines be administered using a 3-dose schedule in immunocompromised populations according to existing age guidelines – NACI Evidence Grade B Recommendation for HPV2 and HPV4 vaccine (fair evidence to recommend immunization); NACI Evidence Grade I Recommendation for HPV9 vaccine (insufficient evidence in either quantity and/or quality to make a recommendation, however other factors may influence decision-making).

While NACI's recommendation regarding HPV2 and HPV4 vaccines in this population remains unchanged, based on the Literature Review conducted to inform these recommendations the Evidence Grade on which the recommendation is based has been upgraded from a Grade I (insufficient evidence in either quantity and/or quality to make a recommendation, however other factors may influence decision-making) to a Grade B (fair evidence to make a recommendation). Evidence does not suggest there are any unique safety concerns in using HPV2 or HPV4 vaccines for immunocompromised populations. There are currently no studies directly evaluating the immunogenicity, efficacy, or safety of HPV9 vaccine in immunocompromised populations with either a 3-dose or a 2-dose schedule (therefore the Evidence Grade on which the recommendation is based is Grade I). However, there is no evidence to suggest that individuals would respond differently to HPV9 vaccine compared to either HPV2 or HPV4 vaccines. As further evidence becomes available, the grade of this recommendation may change.

There are currently no published studies exploring a 2-dose HPV immunization schedule in immunocompromised populations. NACI concludes that there is fair evidence demonstrating that the immunogenicity of HPV2 and HPV4 vaccines can be diminished in immunocompromised populations following a 3-dose immunization schedule, although the antibody responses still typically exceed those resulting from natural infection in immunocompetent individuals. Therefore, although the immunogenicity and efficacy have not been fully characterised in all immunocompromised populations, individuals who are immunocompromised are expected to derive benefit from these vaccines and NACI continues to recommend vaccination of these groups using a 3-dose schedule to provide protection.

Table 1 summarizes the above recommendations according to when to give HPV vaccine and to whom. HPV immunization may be completed with HPV2, HPV4 or HPV9 vaccines in females and HPV4 or HPV9 vaccines in males, according to the immunization schedules summarized in this table. Where possible, the same vaccine should be used to complete the series. If completion of the series with the same vaccine is not possible, the HPV2, HPV4 or HPV9 vaccine may be used to complete the series in females and the HPV4 or HPV9 vaccine may be used to complete the series in males. The HPV9 vaccine among immunocompetent 9 to 26 year olds is expected to provide similar protective efficacy against genotypes contained in the HPV4 vaccine. Moreover, HPV9 vaccine protects against the additional five HPV types not contained in HPV4 vaccine (HPV 31, 33, 45, 52 and 58).

Table 1: NACI Recommendations for the HPV Immunization Schedule

Recommended groups	Recommended immunization schedule	HPV vaccines and NACI Evidence Grade (7)
Healthy (immunocompetent, non-HIV infected) females 9-14 years of age (and healthy females ≥15 years of age in whom the first dose was administered between 9-14 years of age)	2- or 3-dose schedule	HPV2 or HPV4 (Grade A) HPV9 (Grade B)
Healthy (immunocompetent, non-HIV infected) females ≥15 years of age	3-dose schedule	HPV2 or HPV4 (Grade A) or HPV9 (Grade B)
Healthy (immunocompetent, non-HIV infected) males 9-14 years of age (and healthy males ≥15 years of age in whom the first dose was administered between 9-14 years of age)	2- or 3-dose schedule	HPV4 or HPV9 (Grade B)
Healthy (immunocompetent, non-HIV infected) males ≥15 years of age	3-dose schedule	HPV4 or HPV9 (Grade B)
Immunocompromised individuals and immunocompetent HIV infected individuals	3-dose schedule	HPV2 or HPV4 in females (Grade B); HPV4 in males (Grade B); HPV9 in females or males (Grade I)

Efforts should be made to administer HPV vaccines at the recommended intervals. When an abbreviated schedule is required, minimum intervals between vaccine doses should be met. In a 3-dose schedule, the minimum interval between the first and second doses of vaccine is four weeks, the minimum interval between the second and third doses of vaccine is 12 weeks and the minimum interval between the first and last doses in either a 2-dose or 3-dose schedule is 24 weeks.

Authors' statement

The NACI Statement summarized in this article was prepared by Dr. M. Tunis, Dr. S. Ismail, Dr. S. Deeks and approved by NACI.

Conflict of interest

None.

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HPV Working Group Members: Dr. S. Deeks (Chair), Dr. E. Castillo, Dr. S. Dobson, Dr. M. Krajden, Dr. G. Ogilvie and Dr. C. Sauvageau

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Liaison Representatives: Dr. J. Blake (Society of Obstetricians and Gynaecologists of Canada), Dr. J. Brophy (Canadian Association for Immunization Research and Evaluation [CAIRE]), Dr. A. Cohn (Centers for Disease Control and Prevention, United States), Ms. T. Cole (Canadian Immunization Committee), Dr. J. Emili (College of Family Physicians of Canada), Dr. M. Lavoie (Council of Chief Medical Officers of Health), Dr. C. Mah (Canadian Public Health Association), Dr. D. Moore (Canadian Paediatric Society), Dr. A. Pham-Huy (Association of Medical Microbiology and Infectious Disease [AMMI] Canada) and Ms. T. Cole (Canadian Immunization Committee)

Former Liaison Representatives: Ms. E. Sartison (Canadian Immunization Committee)

Ex-Officio Representatives: Dr. (LCdr) K. Barnes (National Defence and the Canadian Armed Forces), Ms. G. Charos (Centre for Immunization and Respiratory Infectious Diseases [CIRID], Public Health Agency of Canada [PHAC]), Dr. G. Coleman (Biologics and Genetic Therapies Directorate [BGTD], Health Canada [HC]), Dr. J. Gallivan (Marketed Health Products Directorate [MHPD], HC), Ms. J. Pennock (CIRID, PHAC), Dr. T. Wong (First Nations and Inuit Health Branch [FNIHB], HC)

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Treatment update for hepatitis C virus-Genotype 3

Source: Johnson SW, Thompson DK, Raccor B. Hepatitis C Virus-Genotype 3: Update on Current and Emergent Therapeutic Interventions. Curr Infect Dis Rep. 2017 Jun;19(6):22. Available from: https://link.springer.com/article/10.1007/s11908-017-0578-5.

PURPOSE OF REVIEW: Direct-acting antiviral agents (DAAs) have markedly improved the prognosis of hepatitis C virus (HCV)-genotype 3 (GT3), a highly prevalent infection worldwide. However, in patients with hepatic fibrosis, cirrhosis, or hepatocellular carcinoma (HCC), GT3 infection presents a treatment challenge compared with other genotypes. The dependence of the HCV life cycle on host lipid metabolism suggests the possible utility of targeting host cellular factors for combination anti-HCV therapy. We discuss current and emergent DAA regimens for HCV-GT3 treatment. We then summarize recent research findings on the reliance of HCV entry, replication, and virion assembly on host lipid metabolism.

RECENT FINDINGS: Current HCV treatment guidelines recommend the use of daclatasvir plus sofosbuvir (DCV/SOF) or sofosbuvir plus velpatasvir (SOF/VEL) for the management of GT3 based upon clinical efficacy [≥88% overall sustained virological response (SVR)] and tolerability. Potential future DAA options, such as SOF/VEL co-formulated with GS-9857, also look promising in treating cirrhotic GT3 patients. However, HCV resistance to DAAs will likely continue to impact the therapeutic efficacy of interferon-free treatment regimens. Disruption of HCV entry by targeting required host cellular receptors shows potential in minimizing HCV resistance and broadening therapeutic options for certain subpopulations of GT3 patients. The use of cholesterol biosynthesis and transport inhibitors may also improve health outcomes for GT3 patients when used synergistically with DAAs. Due to the morbidity and mortality associated with HCV-GT3 infection compared to other genotypes, efforts should be made to address current limitations in the therapeutic prevention and management of HCV-GT3 infection.

Viruses that infect bacteria

Source: Navarro F, Muniesa M. Phages in the Human Body. Front Microbiol. 2017 Apr 4;8:566. eCollection 2017. Available from: https://doi.org/10.3389/fmicb.2017.00566.

Bacteriophages, viruses that infect bacteria, have re-emerged as powerful regulators of bacterial populations in natural ecosystems. Phages invade the human body, just as they do other natural environments, to such an extent that they are the most numerous group in the human virome. This was only revealed in recent metagenomic studies, despite the fact that the presence of phages in the human body was reported decades ago. The influence of the presence of phages in humans has yet to be evaluated; but as in marine environments, a clear role in the regulation of bacterial populations could be envisaged, that might have an impact on human health. Moreover, phages are excellent vehicles of genetic transfer, and they contribute to the evolution of bacterial cells in the human body by spreading and acquiring DNA horizontally. The abundance of phages in the human body does not pass unnoticed and the immune system reacts to them, although it is not clear to what extent. Finally, the presence of phages in human samples, which most of the time is not considered, can influence and bias microbiological and molecular results; and, in view of the evidence, some studies suggest that more attention needs to be paid to their interference.

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Public Health Agency of Canada
130 Colonnade Road
Address Locator 6503B
Ottawa, Ontario K1A 0K9
ccdr-rmtc@phac-aspc.gc.ca

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